

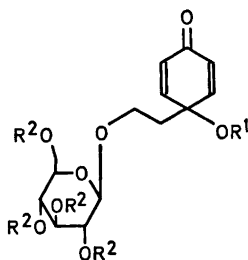
A Quinol Glucoside Isolated from *Cornus* Species

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A glucoside, with a chemical structure novel in type to constituents of higher plants, has been isolated by column chromatography from an aqueous, flavonoid-free extract of autumn foliage of the North American dogwood *Cornus femina* Miller. The non-crystalline glucoside, C₁₄H₂₀O₈, has been assigned the structure *1* on the following evidence.

UV, [λ_{\max} (EtOH) 227 nm (ϵ 9400)]; IR, [λ_{\max} (KBr) 1618, 1663 cm⁻¹], and ¹H NMR data (see Experimental) were



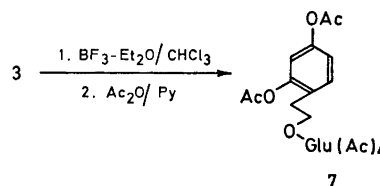
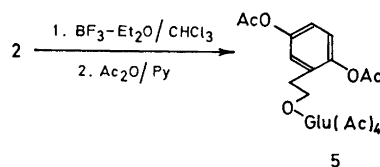
- 1 $R^1 = R^2 = H$
2 $R^1 = H, R^2 = Ac$
3 $R^1 = R^2 = Ac$

all in accord with those expected for structure *1*.^{*} Acetylation, with Ac₂O in pyridine, afforded a tetraacetate *2*, and a penta-

^{*} 4-Hydroxy-4-methyl-cyclohexa-2,5-dienone exhibits absorption maxima at λ 226 nm (ϵ 17 760) (EtOH) in the UV,¹ and at 1617 and 1673 cm⁻¹ (CHCl₃) in the IR region.²

acetate *3*, both syrupy, exhibiting, as parts of their ¹H spectra, signals virtually coinciding with those of methyl tetra-*O*-acetyl- β -D-glucopyranoside, save for the anomeric proton. Emulsin-catalyzed hydrolysis of *1* proceeded easily to give glucose and the aglucone, isolated as the non-crystalline diacetate *4*, exhibiting the expected NMR signals.

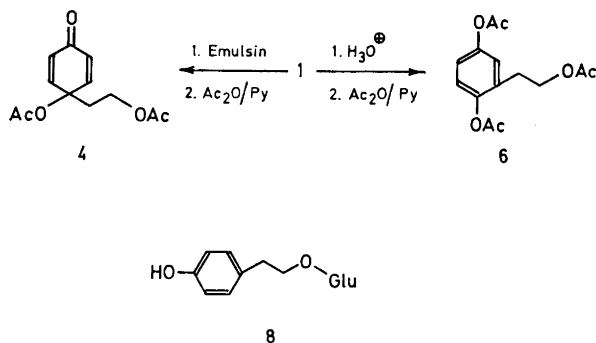
Additional chemical evidence in support of structure *1* was provided by BF₃-induced rearrangement² of *2* to give, after acetylation, the expected hydroquinone glucoside acetate *5*, as colourless crystals. Similarly, acid-catalyzed hydrolysis of *1*,



followed by acetylation, afforded homogentisyl triacetate *6* as the major product. On treatment with BF₃-etherate in CHCl₃, *3* underwent quinol ester-phenol rearrangement² to give, after acetylation, the resorcinol glucoside acetate *7*.

The genus *Cornus* (*sensu* Wangerin) comprises 46 species, 32 of which compose the subgenus *Thelycrania* Endl.³ In the present work, 17 of the latter were studied and invariably found to contain *1*. Conversely, none of 7 studied species, belonging to 4 other subgenera,³ contained *1* in detectable amounts. Taxonomically interesting, the occurrence of *1* and of iridoid glucosides, studied in parallel on the 24 *Cornus* species, appears to be mutually exclusive.

Salidroside, *8*, formerly known from species of *Salix*⁴ and several other genera,



was consistently encountered as a minor congener of 1.

A full account of the distribution of 1 and iridoids within the *Cornus* group will appear elsewhere.

Experimental. Ultraviolet spectra were measured in EtOH; ¹H NMR spectra were recorded on a Varian HA-100 instrument in CDCl₃-solution with TMS as an internal reference, when not otherwise indicated. For TLC, silica gel PF₂₅₄ (Merck) was employed; preparative separations were performed on 20 × 40 cm plates, coated with 1 mm thick layers of silica gel. Detection in UV light.

Isolation of glucoside 1. Frozen foliage (350 g) of *C. femina* (collected in September 1971 and stored at -28° in polyethylene bags) was homogenized in ethanol (1.0 l). After filtration, the filter cake was treated similarly with another 0.5 l portion of ethanol. The combined filtrates were concentrated *in vacuo* to 150 ml. The remaining solution was extracted with two 500 ml portions of ether. The ether solutions were discarded. The aqueous phase was filtered through a column of alumina (300 g),⁵ followed by washing of the column with water (1 l). The combined filtrates were passed through a filter bed of charcoal (175 g) and Celite (200 g), placed in a 22 cm Büchner funnel. The adsorbed glycosides were washed free of carbohydrates with 4 l of water. Elution with 50 % EtOH (2 l) and then 66 % EtOH (0.75 l), followed by concentration of the eluates *in vacuo*, afforded a crude glycoside fraction (5.7 g).

Repeated column chromatography on silica gel, with BuOH:MeOH:H₂O (7:1:3) as the mobile phase, yielded a fast-running glycoside (fraction a, see below) in addition to the sirupy,

chromatographically homogeneous glycoside 1 (3 g). After thorough drying (over P₂O₅), the material was used for further characterization: [α]_D²² -23° (c 1.6, EtOH); the ¹H NMR spectrum (in D₂O, TMS as external reference) exhibited signals at: 7.44 and 6.59 (4H, vinylic, composing an AA'BB' system; J_{AB} 10.5 Hz), 4.71 (1H, anomeric proton H-1', d, J 7 Hz), 2.48 (2H, t, J=7 Hz), and 3.40-4.50 ppm (8H, consisting of 2H from the aglucone, and the 6 non-anomeric, carbon-bound protons of the glucose moiety).

Acetates of 1. Acetylation of 1 (1.0 g) was performed in pyridine (10 ml) with acetic anhydride (5 ml) at room temperature. After 18 h, work-up in the usual way yielded a mixture of two acetates (1.39 g), separated on chromatography (in ether) into a slow- and a faster-running component.

The former, consisting of 2 (203 mg), was thoroughly dried before analysis. (Found: C 52.35; H 6.20. Calc. for C₂₂H₂₈O₁₂: C 52.17; H 6.13). [α]_D²² -26° (c 3.6; EtOH); λ_{max} 227 nm (ε 10 600); NMR-data: 6.92 and 6.16 (2 × 2H, vinylic), 5.40-4.90 (3H; H-2', H-3', H-4'), 4.56 (1H, H-1', d, J 7.5 Hz), 4.27 and 4.23 (2H, H-6'), 4.08 and 3.71 (2 × 1H; A and B part of an ABX₂-system, ca 3.75 (1H, H-5'), 3.37 (1H, OH), and 2.13-2.00 ppm (14H, 4 OAc plus CH₂).

The pentaacetate, 3 (532 mg), was analyzed after drying. (Found: C 54.57; H 5.59. Calc. for C₂₄H₃₀O₁₃: C 54.75; H 5.74). [α]_D²² -18.0° (c 2.0; EtOH); λ_{max} 239 nm (ε 9800). NMR-data: 6.90 and 6.28 (4H, vinylic), 5.35-4.85 (3H; H-2', H-3', H-4'), 4.52 (1H, H-1', d, J 7.5 Hz), 4.28 and 4.23 (2H, H-6'), 3.99 and 3.61 (each 1H; A and B part of an ABX₂-system, J_{AB} 10.5 Hz, J_{AX} = J_{BX} = 6 Hz), ca. 3.75 (1H, H-5'), 2.18 (2H, t, X₂-part of an

ABX₂-system), and 2.15–2.03 ppm (15H; 5 OAc).

Enzymic hydrolysis of 1. A mixture of **1** (408 mg), emulsin (190 mg), and water (10 ml) was stirred overnight at room temperature. The filtered solution was extracted with three 10 ml portions of BuOH; the solvent was removed *in vacuo*, and the residue was subjected to acetylation (with Ac₂O in pyridine). From the resulting product mixture (175 mg), a homogeneous, non-crystalline product, consisting of **4**, was isolated by chromatography with C₆H₆:Et₂O (1:1) as the mobile phase. (Found: C 60.38; H 5.82. Calc. for C₁₂H₁₄O₆: C 60.50; H 5.92.) λ_{\max} 239 nm (ϵ 7100); NMR-data: 6.88 and 6.28 (each 2H, composing an AA'BB'-system), 4.18 (2H, t, *J* 6.5 Hz), 2.19 (2H, t, *J* 6.5 Hz), 2.08 and 2.03 ppm (2 × 3H; 2 OAc).

In the above aqueous solution, the presence of glucose was demonstrated by paper-chromatographic analysis and comparison with an authentic specimen, in (i) BuOH:EtOH:H₂O (4:1:3), and (ii) BuOH:Py:H₂O (6:4:3).

Rearrangement of 2. A solution of the tetraacetate **2** (250 mg) in CHCl₃ (5 ml) was treated with BF₃·Et₂O (150 mg) for 3 h at room temperature. An excess of NaHCO₃-solution was added, and the mixture was extracted with CHCl₃. The crude reaction product (270 mg) was purified by chromatography (ether as an eluent) to give the rearranged product (131 mg). Acetylation, with Ac₂O in pyridine, afforded the hexaacetate **5** (157 mg), which was recrystallized from MeOH, m.p. 136–137.5°. (Found: C 54.94; H 5.76. Calc. for C₂₆H₃₂O₁₄: C 54.92; H 5.67) $[\alpha]_{D}^{22}$ –16.0° (*c* 3; CHCl₃). λ_{\max} 267 (ϵ 600) and 272 nm (ϵ 560). NMR-data: 7.0 (3H, s, arom.), 2.81 (2H, t, *J* 7 Hz, benzylic CH₂), 2.31 and 2.29 (2 × 3H, phenolic OAc); 2.09, 2.02, 1.99, and 1.96 ppm (4 × 3H, aliphatic OAc).

Rearrangement of 3. The pentaacetate **3** (129 mg) was dissolved in CH₂Cl₂ (10 ml), and two drops of BF₃·Et₂O were added. After 5 min at room temperature, the solution was washed with two 5 ml portions of a NaHCO₃-solution. After drying, and concentration to dryness, the residue was reacylated (Ac₂O in pyridine) to give a mixture of products (99 mg), from which **7** was isolated as the major product (66 mg) by chromatography in Et₂O. (Found: C 55.01; H 5.55. Calc. for C₂₆H₃₂O₁₄: C 54.93; H 5.67.) $[\alpha]_{D}^{22}$ –11° (*c* 2.1, EtOH); λ_{\max} 266 (ϵ 560) and 271 nm (ϵ 580). NMR-data: 7.26 (1H, dd, *J* 9 Hz and *ca.* 1 Hz, arom.), 7.01–6.88 (2H, arom.), 2.83 (2H, t, *J* 6.5 Hz, benzylic CH₂), 2.32 and 2.27 (2 × 3H, phenolic OAc), and 2.10–1.95 ppm (4 × 3H, aliphatic OAc).

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Acid hydrolysis of 1. The glucoside **1** (138 mg) was dissolved in 3% H₂SO₄ (5.5 ml) and heated on a steam-bath for 48 h. Ether extraction (5 × 10 ml) afforded the aglucone (34 mg), which was subjected to acetylation (Ac₂O in pyridine) for 2 h at r.t. and worked up in the usual way to give a crude product (43 mg), which was purified by chromatography (pentane-ether, 5:2) to give a homogeneous specimen (30 mg) of homogentisyl acetate **6**. (Found: C 60.08; H 5.76. Calc. for C₁₄H₁₆O₆: C 59.99; H 5.75.) λ_{\max} 217 (ϵ 5500), 268 (ϵ 575), and 273 nm (ϵ 550). NMR-data: 7.09 (3H, s, arom.), 4.28 (2H, t, *J* 7.5 Hz), 2.89 (2H, t, *J* 7.5 Hz, benzylic CH₂), 2.34 and 2.29 (2 × 3H, phenolic OAc), and 2.04 ppm (3H, aliphatic OAc).

Isolation of salidroside, 8. Fraction **a**, from the glucoside isolation, was freed of less polar contaminants by extraction with three 50 ml portions of EtOAc. The aqueous solution was taken to dryness *in vacuo*, and the residue was subjected to acetylation (Ac₂O, pyridine, 2 days). Repeated chromatography (Et₂O as the eluent) gave a fraction (98 mg) which, according to NMR analysis, was rich in salidroside acetate. Deacetylation, with NH₃ in MeOH, yielded a crude glucoside, which was purified by chromatography (in CHCl₃:MeOH, 4:1) to give a homogeneous fraction. On trimethylsilylation a product was formed, possessing an NMR-spectrum, indistinguishable from that of persilylated salidroside.⁸

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